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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/469,812	12/22/1999	MAARTEN H. STUIVER	SYN-014	5404

28393 7590 10/01/2004

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EXAMINER

KRUSE, DAVID H

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/469,812

Applicant(s)

STUIVER ET AL.

Examiner

David H Kruse

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-6,8,9 and 11-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-6,8,9 and 11-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

STATUS OF THE APPLICATION

1. This Office action is in response to the Amendment and Remarks filed 12 July 2004.
2. As outlined in the Interview Summary mailed 22 June 2004, entry of claim 12 is accepted by the Examiner because of Applicant's intention to initiate an interference with issued patent U.S. 6,521,458.
3. The Examiner notes that Applicant has submitted new claims 14-29 under 37 C.F.R. § 1.607(c). The Examiner also notes that Applicant has presented an incomplete response under 37 C.F.R. § 1.607(a)(5) because Applicant has failed to state how each term of the copied claim(s) is supported by the specification.
4. Formal drawings were received on 17 February 2004. These drawings are acceptable.
5. Claim 5 is now in compliance with the Sequence Rules.
6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

7. Claim 2 remains objected to and claim 13 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This objection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. Applicant's arguments filed 12 July 2004 have been fully

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considered but they are not persuasive. Applicant argues that the objection to claim 2 as needing "and" delineators for separating the species is rendered moot by the cancellation of the second species set, which has been listed in new dependent claim 13 (page 12, 3rd paragraph of the Remarks). This argument is not found to be persuasive because it does not address the issue that claim 2, and new claim 13, are broader in scope than claim 1, which recites "a gene encoding a toxin gene and/or a nucleotide sequence that interferes with DNA unwinding" wherein the specification does not teach that the limitation "an antisense sequence for a housekeeping gene" meets the limitations of claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. Claims 20 and 29 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner can find no written description support for the limitation "wherein the lethal polynucleotide sequence is within about 5 kb of the left border" in the specification, and Applicant has failed to state how each term of the copied claim(s) is supported by the specification under 37 C.F.R. § 1.607(a)(5). This is a New Matter rejection.

9. Claims 1, 4, 6 and 8-11 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. Applicant's arguments filed 12 July 2004 have been fully considered but they are not persuasive.

Applicant's arguments as they are directed to the description of "a gene encoding a toxin gene" are found to be persuasive. The instant rejection is maintained to the extent that the instant claims are directed to "a nucleotide sequence that interferes with DNA unwinding" as broadly claimed.

Applicant argues that it is irrelevant that the specific sequence of each toxin or each nucleotide sequence that interferes with DNA unwinding is not listed as such specificity is not necessary to fulfill the written description requirement (page 13, 4th paragraph of the Remarks). This argument as directed to "toxin" has been conceded by the Examiner. This argument, as directed to nucleotide sequences that interfere with DNA unwinding, is not found to be persuasive because the function of such a genus of nucleotide sequences does not adequately describe the structure required to practice the claimed invention.

Applicant argues that the structure of the vectors of the claimed invention are clearly related to their function, and as described in the specification, the structure of the vectors of the claimed invention eliminates the problem of plant transformants that have more vector sequence other than the T-DNA sequence (page 14, 2nd paragraph of the Remarks). This argument is not found to be persuasive because, while the structure of

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a vector used to transform plants is recognized by the art in general terms, the function of a nucleotide sequence that interferes with DNA unwinding is not generally recognized by the art as related to a specific structure.

10. Claims 1, 2, 4, 8, 9 and 11 remain rejected and claim 13 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. This rejection has been modified in view of Applicant's arguments, and is directed to the enablement of a vector comprising a nucleotide sequence that interferes with DNA unwinding or an antisense sequence for a housekeeping gene. To the extent that the instant claims are directed to a vector, and methods of using same comprising a gene encoding a toxin, comprising a specific vir box sequence or comprising a sequence of 20-60 basepairs with a GC content of more than 80%, the Examiner finds Applicant's arguments persuasive. Applicant's arguments filed 12 July 2004 have been fully considered but they are not persuasive as they are directed to the remaining issues.

Applicant argues that to enable the claimed invention it is not necessary to list in the specification each toxin gene and/or each nucleotide sequence that interferes with DNA unwinding because such information is readily available to one of skill in the art (page 16, 3rd paragraph of the Remarks). This argument is not found to be persuasive as directed to "nucleotide sequence that interferes with DNA unwinding" because one of

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skill in the art at the time of Applicant's invention could not have recognized the required function of a nucleic acid sequence as interfering with DNA unwinding without an actual reduction to practice, especially nucleic acid sequences that would properly function in a vector for plant transformation.

Applicant's arguments on page 16, 4th paragraph to page 17, 2nd paragraph are found to be irrelevant to the instant rejection because the Examiner does not argue that vectors for plant transformation comprising a T-DNA sequence are not adequately known in the art. What is at issue is a nucleotide sequence that interferes with DNA unwinding used in a vector for plant transformation as broadly claimed.

Applicant argues that any experimentation that may be needed to practice the full breadth of the claims would not be unreasonable, and that there is ample support both in the application itself and in the literature guiding the skilled artisan on genetic manipulation techniques to make and use the vectors and plant hosts of the present invention (page 18, 4th paragraph of the Remarks). As directed to the instant claims as they read on the use of a nucleotide sequence that interferes with DNA unwinding, the Examiner maintains that it would have required undue trial and error experimentation by one of skill in the art at the time of the invention to make and use a vector for plant transformation comprising a nucleotide sequence that interferes with DNA unwinding as broadly claimed because one of skill in the art would have been required to identify such nucleotide sequences, and introduce them into a vector for plant transformation at various locations to identify those nucleic acid sequences and vector locations that

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would prevent incorporation of vector backbone sequences, which Applicant asserts is what makes the instant invention useful.

The issue of undue trial and error experimentation remains as it is directed to the instant claims to the extent that they read on the use of an antisense sequence for a housekeeping gene.

11. Claims 1, 2, 4, 5, 6, 8 9 and 11 remain rejected and claim 13 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. Applicant's arguments filed 12 July 2004 have been fully considered but they are not persuasive.

At claim 1, it remains unclear where "a gene encoding a toxin gene and/or a nucleotide sequence that interferes with DNA unwinding" is located in relation to "a sequence located between two direct repeats" within the claimed vector. Hence, it remain unclear what the metes and bounds of the invention are. Applicant argues that amending the claim to recite that the gene or nucleotide sequence is not located within the T-DNA sequence (page 19, 4th paragraph of the Remarks). The Examiner does not find this argument persuasive, and the amendment to claim 1 does not obviate the instant rejection. The specification states that the invention comprises a vector for plant transformation characterized in that the vector further comprises a nucleic acid sequence which prevents the development of plant transformants having more vector sequence than the T-DNA sequence (page 2, 4th paragraph of the specification).

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Hence, it appears, due to the nature of the invention, that the gene encoding a toxin or a nucleotide sequence that interferes with DNA unwinding must be located outside of the left T-DNA border, or else plant transformants would have more vector sequence than the T-DNA sequence.

Claim Rejections - 35 USC § 102

12. Claims 1, 2, 8 and 11 remain rejected and claims 12 and 14-29 are rejected under 35 U.S.C. § 102(g) as being anticipated by Gutterson *et al* (U.S. Patent No. 6,521,458, filed 30 April 1999, which claims benefit of U.S. Provisional Application 60/086,440, filed 22 May 1998). Applicant has stated that new claims 14-29 have been copied from U.S. Patent 6,521,458 (page 9, 4th paragraph of the Remarks). This rejection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. Applicant's arguments filed 12 July 2004 have been fully considered but they are not persuasive.

Applicants state that they in no way disclaimed the subject matter of the claim presented by the Examiner for copying and in no way conceded that the patentee was the first to invent the subject matter set forth in the claim presented to be copied (page 20, 2nd paragraph of the Remarks). The Examiner notes Applicant's assertion.

Applicants argue that if they are found to have disclaimed the subject matter contained in the claim suggested by the Office, claims 1, 2, 8 and 11 are not anticipated by Gutterson. Applicants argue that if it is found that Gutterson invented the species listed in the suggested claim prior to Applicants inventing that species, there is no evidence that Gutterson invented the genus or any other species prior to the Applicants,

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and that the Office has not established that the species set forth in the suggested claim actually anticipates claims 1, 2, 8 and 11 (page 20, 3rd paragraph of the Remarks). This argument is not found to be persuasive because the prior art does not need to anticipate all of the species of a claim. The species, gene encoding a barnase toxin, anticipates the toxin encoding gene genus of the instant claims. Possession of the claimed genus would require substantial evidence by Applicant of prior possession of the broad genus, See MPEP § 715.03. In the case of a small genus such as the halogens, which consists of four species, a reduction to practice of three, or perhaps even two, species might show possession of the generic invention, while in the case of a genus comprising hundreds of species, reduction to practice of a considerably larger number of species would be necessary. In cases where predictability is in question, on the other hand, a showing of prior completion of one or a few species within the disclosed genus is generally not sufficient to overcome the reference or activity. *In re Shokal*, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). In the instant case Applicant has only reduced to practice the same species as the prior art and has not provided evidence that they have reduced to practice any other species.

Applicant argues that Gutterson is not prior art because Gutterson claims priority to a provisional application filed May 22, 1998, and the instant Application claims priority [under 35 U.S.C. § 119 (a)-(d)] to EP 97201990.1 filed 30 June 1997). This argument is not found to be persuasive because 35 U.S.C. § 102(g)(2) states “the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it”. Because Applicant failed to timely respond to the copy claim in the Office

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action mailed 28 March 2001, the Examiner has considered Applicant to have disclaimed the invention suggested in the copy claim (see MPEP § 2305.02). See also MPEP § 2308.01.

Applicant argues that Gutterson must teach each and every element of the claim to anticipate (pages 21-22 of the Remarks). This argument is not found to be persuasive because the limitations of claim 1 are in the alternative. See MPEP § 2131, which states that "When a claim covers several structures or compositions, either generically or as alternatives, the claim is deemed anticipated if any of the structures or compositions within the scope of the claim is known in the prior art." *Brown v. 3M*, 265 F.3d 1349, 1351, 60 USPQ2d 1375, 1376 (Fed. Cir. 2001).

Applicants argue that they did not refuse to copy the claim verbatim but, rather, did not copy the claim verbatim because of extraordinary circumstances that were beyond Applicants' control (page 23, 2nd paragraph of the Remarks). This argument is not found to be persuasive. See MPEP § 2305.02, which states, "Should any one of the applicants fail to present the claim or claims suggested within the time specified, all claims not patentable thereover are rejected on the ground that the applicant has disclaimed the invention to which they are directed. If the applicant presents the suggested claims later they will be rejected on the same ground. See MPEP § 706.03(u).".

The Examiner notes that the Office of Petitions in the response mailed 17 July 2002 denied entry of the copy claims suggested in the Office action mailed 28 March 2001. The Office of Petitions states, "The present facts present issues which are

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appropriately under the jurisdiction of the examiner and the Board of Appeals, and not the Office of Petitions.” (page 1 of the Petition Decision mailed 17 July 2002). The Examiner has allowed entry of new claims 12 and 14-29 under 37 C.F.R. § 1.607, but maintains that the instant claims are anticipated.

Claim Rejections - 35 USC § 103

13. Claim 9 remains rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,421,458, filed 30 April 1999, Gutterson *et al.* This rejection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. Claims 1, 2, 8 and 11 have been withdrawn from the instant rejection because they have been found to be anticipated by Gutterson *et al.* Applicant's arguments filed 12 July 2004 have been fully considered but they are not persuasive.

Applicant argues that reliance on the entire teaching of Gutterson is improper (paragraph spanning pages 23-24 of the Remarks). This argument is not found to be persuasive as outlined supra.

14. Claims 1, 4, 5, 9 and 11 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Ramanathan *et al.* (Plant Molecular Biology 1995, 28: 1149-1154) in view of D'Souza-Ault *et al.* (1993, J. Bacteriology 175(11): 3486-3490). This rejection is repeated for the reason of record as set forth in the last Office action mailed 1 October 2003. Applicant's arguments filed 12 July 2004 have been fully considered but they are not persuasive.

Applicant argues that neither Ramanathan nor D'Souza-Ault, neither individually nor in combination, teach or suggest a vector for plant transformation comprising a T-

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DNA sequence, the T-DNA sequence comprising a sequence located between two direct repeats, and a gene encoding a toxin gene and/or a nucleotide sequence that interferes with DNA unwinding, or methods of using such a vector. Applicant argues that Ramanathan teaches only that "it would be desirable to incorporate into a (sic) T-DNA vectors a 'stop-transfer' signal adjacent to the left border" and that Ramanathan does not teach or even suggest including a toxin gene (paragraph spanning pages 24-25 of the Remarks). This argument is not found to be persuasive because Ramanathan teaches the problem of incorporation of vector sequences beyond the left T-DNA border when transforming plants, and suggests incorporating a 'stop-transfer' signal adjacent to the left border.

Applicant argues that D'Souza-Ault does not cure the deficiencies of Ramanathan, because D'Souza-Ault is a bacteriology reference that describes the identification of a specific Ros binding sequence in the promoter region of the virC and virD operons of Agrobacterium, and that D'Souza-Ault is silent regarding vectors for plant transformation, and methods for their use (page 25, 2nd paragraph of the Remarks). This argument is not found to be persuasive because D'Souza-Ault teaches a naturally occurring nucleotide sequence that would interfere with DNA unwinding, that being the Vir box and that VirG acts as a repressor. Given the general knowledge in the art at the time of the invention, one of ordinary skill in the art would have been motivated to use the Vir box sequence in a T-DNA construct adjacent to the left T-DNA border as suggested by Ramanathan to repress integration of vector sequence into a transformed plant. One of ordinary skill in the art would have understood that a repressor prevents

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DNA unwinding. Given the teachings of D'Souza-Ault that the Vir box sequence can be used as a repressor sequence, one of ordinary skill in the art would have had a reasonable expectation of success in modifying the teachings of Ramanathan.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.



DAVID H. KRUSE, PH.D.
PATENT EXAMINER

David H. Kruse, Ph.D.
23 September 2004

18. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.